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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/888,313	06/22/2001	Ian Tomlinson	8039/1122	9556

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EXAMINER	
SHIBUYA, MARK LANCE	

ART UNIT	PAPER NUMBER
1639	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/888,313	TOMLINSON ET AL.	
	Examiner	Art Unit	
	Mark L. Shibuya, Ph.D.	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *56-68 and 78-86* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *56-68 and 78-86* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/17/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Application 09888313, (20020055110 A1): Claims 56-68 and 78-86 are pending and examined. It is respectfully noted that claims 69-77 and 87-117 were canceled by examiner's amendment, as authorized on 2/2/2006.

2. The examiner of record has changed.

Continued Examination Under 37 CFR 1.114

3. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after allowance or after an Office action under *Ex Parte Quayle*, 25 USPQ 74, 453 O.G. 213 (Comm'r Pat. 1935). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 8/17/2007 has been entered.

Petition

4. The petition decision, mailed 8/20/2007, granting withdrawal of the instant application from issue, is acknowledged again.

Priority

5. This application, 09/888,313, filed 6/22/2001, claims benefit of 60/246,851, filed November 8, 2000. This application claims foreign priority to UK 0015443.5 filed June 23, 2000 and UK 0026099.2 filed October 25, 2000.

Information Disclosure Statement

6. The information disclosure statement (IDS) submitted on 8/17/07 was filed after the mailing date of the notice of allowance on 2/10/2006. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement was considered by the examiner.

Specification

7. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: There is no recitation of the term "control sequence", (claim 79); the term "operatively linked", (claim 79); "naked or complexed nucleic acid", (claim 85) in the body of the specification as filed.

Claim Rejections - 35 USC § 112, First Paragraph

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 56-68 and 78-86 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is for new matter.

The specification as filed does not provide support for a first repertoire and a second repertoire, each comprising a heavy or light chain polypeptide. Furthermore, the specification as filed does not provide support for the genera of "heavy or light chain polypeptides", although the specification discloses heavy and light chain of antibodies.

Claim Rejections - 35 USC § 112, Second Paragraph

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 56-68 and 78-86 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "continuous lines" in claim 56, 57, 63, 67 and 68 is a relative term which renders the claim indefinite. The term "continuous line" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The present specification defines a line as preferably "XX long and YY wide" which can be straight, curved, circles, polygons, radial lines, stream,

channel, flow, tubes, tubing, droplets which coalesce, spray, tube with a lumen (please refer to page 4, last paragraph; page 5, page 26, first paragraph). The dimension of "XX" and "YY" would not be readily ascertained by one of skill in the art. For example, a "line" "XX long and YY wide" made of "a series of droplets" that "coalesce" into a "circle" could be a spot; a line could be a centrifuge "tube" with a "lumen into which a member of a repertoire useful in the inventions is placed"; a line could be a streak on a plate, a line could be a lane in a gel, etc.

In addition, the term "juxtaposed" in claims 56, 62, 67, and 67 ("juxtaposing") are relative terms that render the claim indefinite. The term "juxtaposed" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The present specification defines juxtaposition as including "but not limited to physical contact"; separated by no more than 20 μm, 10 μm, or 5 μm; or intersection of lines wherein the lines intersect at between 1° and 179° angle, 45° and 135° angle, 90° angle. For example, a line (e.g. spot) dropped on top of another spot is "juxtaposed" at an angle; a microcentrifuge tube placed within 20 μm of another tube is "juxtaposed", a streaked plate with colonies along the streak are juxtaposed, a lane in a gel within 20 μm of another lane could be juxtaposed, etc.

Claim 56 recites the limitation "a heavy or light chain polypeptide" in lines 2-3. There is uncertain antecedent basis for this limitation in the claim. It is uncertain if this limitation is the same as "a heavy or light chain polypeptide" in lines 1-2.

The terms "heavy" and "light chain polypeptide" in claim 56 are relative terms that render the claim indefinite. The terms are not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree of heaviness or lightness of chains of polypeptides, and one of skill in the art would not be reasonably apprised of the metes and bounds of the claimed invention.

Claim 58 recites the limitation "said heavy or light chain" in lines 1-2. There is uncertain antecedent basis for this limitation in the claim. It is unclear which of the heavy and light chains polypeptides is referred to, (i.e., if the first or second repertoire is referred to).

Claim 64 recites the limitation "a different target antigen" in line 2. There is uncertain antecedent basis for this limitation in the claim. It is unclear as to what the instant target antigen is different from.

Claim 78 recites the limitation "if present, third repertoires" and, "said target epitope", and "said third repertoire" in lines 2, 3-4, and 4, respectively. There is insufficient antecedent basis for this limitation in the claim, in regard to claim 56, and uncertain antecedent basis in regard to claims 62 and 63.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

13. Claims 56-61, 65-68, 78, 79, and 83 are rejected under 35 U.S.C. 102(b) as being anticipated by Biebuyck et al., US 6,089,853, (IDS entered 8/17/2007).

The claims are drawn to a method for screening a first repertoire of members comprising a heavy or light chain polypeptide against a second repertoire of members comprising a heavy or light chain polypeptide to identify those members of the first repertoire which interact with members of the second repertoire, comprising: (a) arranging the first repertoire in at least one first series of continuous lines wherein each line of said first series comprises a member of said first repertoire and arranging the second repertoire in at least one second series of continuous lines wherein each line of said second series comprises a member of said second repertoire, wherein the first and second repertoires form an array, wherein a plurality of said first series of continuous lines intersects with a plurality of said second series of continuous lines, and wherein a plurality of members of the first repertoire are juxtaposed to a plurality of members of the second repertoire; and (b) detecting an interaction between heavy or light chain polypeptides of the first and second repertoires, thereby identifying those members of the first repertoire that interact with members of the second repertoire; and variations thereof.

Biebuyck et al., US 6,089,853, throughout the patent and abstract, and at col. 4, lines 16-39, teach methods of comprising immobilized ligands that are chemically defined bodies (CDBs), such as drugs, enzymes and immunoglobulins, which read on a repertoire of members comprising heavy or light chain polypeptides; wherein the CDBs are stamped or printed in patterns along conduits, reading on continuous lines, and wherein exposure of this substrate to heterogeneous solutions of receptors, reading on a second series repertoire of members that interact with the first repertoire, resulting in specific recognition and attachment of the receptors to the immobilized ligands. Biebuyck et al., at col. 3, line 48-col. 4, line 38, teach stamping of immunoglobulin onto surfaces. Biebuyck et al., state:

> In another application, different types of C-CDBs, in particular ligands or receptors may be deposited simultaneously on a contacted substrate surface. The substrate patterned in this way can be used as a test probe for the receptors and ligands, respectively, to which the C-CDBs are complementary. If the conduit of a first and a second patterning device consist of n parallel channels each which are oriented orthogonal to each other and if the two patterns are transferred sequentially to the substrate, then n.sup.2 combinations of materials can be deposited. High-density DNA, protein or peptide arrays, useful for assaying, can be generated effectively in this way. Also patterns can be generated which are composed of several structures. It is possible, for instance, to deposit two layers on top of each other in the shape of the pattern by rinsing through the conduits two different fluids, one after the other, from which the two layers are precipitated, respectively. It is also possible to rinse a cleaning fluid in between in order to avoid mixing of the two precipitation generating fluids. Rinsing of two fluids in periodic alternation allows the generation of superlattice-type patterned layers by this method. In another application, the first fluid might be corrosive, producing a pattern of grooves which might be filled up with a different material by precipitation from the second fluid. The method can also be used for separation and purification of CDBs in a process of selective affinity chromatography as described in "Guide to protein purification", by Murray P. Deutscher, Academic Press, Vol. 182. This method is general and used extensively in the purification of small and large molecules known in the chemical and biochemical fields.

Biebuyck et al., at col. 7, lines 30-60.

14. Claims 56-58, 60, 62, 63, 64, 65-68, 78, and 79 are rejected under 35 U.S.C. 102(b) as being anticipated by Rowe et al. Anal. Chem. 71(2): 433-439, 1999 (supplied by applicants in IDS).

Rowe et al., throughout the publication, teach methods of producing two-chain or three-chain polypeptides comprising utilizing an array immunosensor wherein vertical channels comprise antibodies labeled with biotin (reading on a first or second repertoire), which binds to avidin, (reading on a first repertoire) and adding samples (reading on a second or third repertoire), flowed through horizontal channels (e.g. single-chain polypeptides; first repertoire and/or second repertoire; continuous lines that may be at 179° angles if two single-chain polypeptides per channel to make VH-VL for example) wherein the vertical and horizontal channels are at 90° angles (please refer to entire reference particularly Figure 1; experimental section).

Therefore, the presently claimed invention is anticipated by the teachings of Rowe et al.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 56-68 and 78-85 are rejected under 35 U.S.C. 103(a) as being unpatentable over either of Biebuyck et al., US 6,089,853, (IDS filed 8/17/2007) or Rowe et al., Anal. Chem. 71(2): 433-439, 1999 (supplied by applicants in IDS), each take separately from the other, and each taken in view of Buechler et al., US Patent 6,057,098, (of record).

Biebuyck et al., US 6,089,853, is relied upon as in the above rejection under 35 USC 102. Rowe et al., is relied upon as in the above rejection under 35 USC 102.

Biebuyck et al., US 6,089,853, (IDS filed 8/17/2007) and Rowe et al., taken separately, do not teach methods comprising a first repertoire comprising VH and a second repertoire comprising VL, and do not teach methods comprising nucleic acid sequences, various expression vectors and hosts thereof.

Buechler et al. disclosed a method of producing a multivalent polypeptide display library that can be use as diagnostic reagents (col. 2, lines 17-18; col. 4, lines 20-24). The polypeptides comprise of a heavy or light chain polypeptide of V_H or V_L sequences (col. 10, lines 53-65). Buechler discloses the method of constructing libraries of antibody fragments comprising light or heavy chain for screening (col. 8, lines 8-11; col. 10, lines 53-65). Thus Buechler teach that two repertoires comprise heavy or light chain polypeptide molecules as claimed in the present method.

Buechler et al., at col. 2, line 15-col. 4, line 19, teach complexing libraries of antibody heavy and light chain to produce multivalent Fab phage display libraries. Buechler et al., at col. 8, line 20-col. 9, col. 18, teach bacteriophage, including M13, (which reads on linear expression vectors) and eukaryotic viruses. Buechler et al., at col. 33, line 55-col. 38, line 25, teach plasmid vectors. Buechler et al., at e.g., col. 17, line 50-col. 18, line 21, teach *E. coli* bacterial hosts, yeast hosts and mammalian cell hosts.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to make and use methods comprising a first repertoire comprising

VH and a second repertoire comprising VL, and do not teach methods comprising nucleic acid sequences, various expression vectors and hosts thereof.

One of ordinary skill in the art would have been motivated to make and use methods comprising a first repertoire comprising VH and a second repertoire comprising VL, and do not teach methods comprising nucleic acid sequences, various expression vectors and hosts thereof, because it would be desirable to produce expression libraries of antibodies and/or their variable regions for affinity screening, to achieve diverse populations, (Buechler et al., e.g., at the abstract).

17. Claim 86 is rejected under 35 U.S.C. 103(a) as being unpatentable over either of Biebuyck et al., US 6,089,853, (IDS filed 8/17/2007) or Rowe et al., Anal. Chem. 71(2): 433-439, 1999 (supplied by applicants in IDS), each take separately from the other, and each taken in view of Buechler et al. (US Patent 6,057,098) as applied to claims 56-68 and 78-85 above, and further in view of Bussow et al. Nucleic Acids Research 26(21): 5007-5008, 1998.

Biebuyck et al., US 6,089,853, (IDS filed 8/17/2007) or Rowe et al., Anal. Chem. 71(2): 433-439, 1999 (supplied by applicants in IDS), each take separately from the other, and each taken in view of Buechler et al. (US Patent 6,057,098) do not teach or suggest methods comprising arraying at least one repertoire using robotic means.

Bussow et al., throughout the publication, teach a picking/gridding robot that gridded onto filter membranes cells expressing proteins (e.g. first, second, and/or third

repertoire of single-chain polypeptides, lines on grid from left to right and/or second repertoire of single-chain polypeptides, lines on grid from top to bottom; juxtaposed; antigen) and adding a "stream" (e.g. line; first, second, and/or third repertoire of single-chain/two-chain polypeptides) of monoclonal antibody thus creating two- or three-chain polypeptides (please refer to entire disclosure particularly page 5007, third and fourth paragraphs; page 5008, third full paragraph).

It would have been *prima facie* obvious, at the time the invention was made, for one of ordinary skill in the art to have made and used methods comprising arraying at least one repertoire using robotic means.

One of ordinary skill in the art would have been motivated to make and use methods comprising arraying at least one repertoire using robotic means because of the desirability of high throughput assaying of libraries, as taught by Bussow et al., at the abstract and p. 5008.

Conclusion

18. Claims 56-68 and 78-86 are rejected. No claims are allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Shibuya, whose telephone number is (571) 272-0806. The examiner can normally be reached on M-F, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Doug Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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